A prospective randomized study to compare neurocognitive outcome after Stereotactic Radiosurgery or Whole Brain Radiation Therapy for the treatment of multiple brain metastases

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55790

Source
ToetsingOnline

Brief title
Cognitive outcome after WBRT or SRS in patients with brain metastases

Condition

- Other condition
- Metastases
- Nervous system neoplasms malignant and unspecified NEC

Synonym
Brain metastases, brain tumor

Health condition

cognitieve stoornissen

Research involving
Human

Sponsors and support

Primary sponsor: Sint Elisabeth Ziekenhuis
Source(s) of monetary or material Support: ZonMw,Elekta Instruments AB

Intervention

Keyword: Brain metastases, Cognitive function, Stereotactic Radiosurgery, Whole Brain Radiation Therapy

Outcome measures

Primary outcome

• Cognitive functioning as assessed with a battery of neuropsychological tests:

The revised Hopkins Verbal Learning Test (HVLT-R), WAIS Digit Span and Digit

Symbol, TMT A and B, COWA, and Grooved Pegboard

Secondary outcome

• Fatigue (MFI)

• Health related QOL (FACT-BR)

• Depression and anxiety (HADS)

• Overall Survival

• Local and distant tumor control

Study description

Background summary

There is a trend to treat multiple brain metastases (BM) with stereotactic radiosurgery (SRS). This is supported by prospective data and the recently published American guideline on BM. In The Netherlands, the standard of care

for patients with multiple metastases (>4) remains whole brain radiotherapy (WBRT). Nonetheless, in our hospital, SRS has been successfully applied in patients with up to 10 BM and occasionally up to 20. SRS is expected to cause fewer cognitive side effects than WBRT. There are no published trials yet directly comparing SRS to WBRT, including objective neuropsychological testing.

Study objective

Primary Objective
Our primary aim is to compare cognitive decline at 3 months, defined as a significant decline (5 point decrease from baseline based on the reliable change index with correction for practice effects) in HVLT-R Total Recall score (verbal learning and memory test) after treatment with either SRS or WBRT in patients with 11-20 non-melanoma BM at time of treatment initiation.

Secondary Objectives
• To determine the magnitude of the cognitive effects at 6, 9, 12, and 15 months follow-up in both treatment arms: improvements and/or declines in memory, executive function, attention, processing speed, and upper extremity fine motor dexterity
• To determine overall survival in both treatment arms
• To determine local and distant tumor control in the brain at 3, 6, 9, 12 and 15 months post treatment
• To assess psychological functioning (fatigue, depression and anxiety) and health related Quality of Life (QOL) in both treatment arms at 3, 6, 9, 12, and 15 months post treatment
• To identify possible predictors of cognitive functioning (age, sex, number and cumulative volume of BM, extracranial disease status, type and duration of systemic and salvage therapies, local and distant control, psychological functioning) after each type of treatment

Study design

Prospective randomized multicenter study with follow-up (cognitive testing) at 3, 6, 9, 12, and 15 months and 3-monthly MRI scans after treatment with either WBRT or SRS.
Groups will be balanced at baseline (prior to radiotherapy), taking into account several (stratification) factors that may influence cognitive functioning over time, such as: cumulative tumor volume in the brain, systemic treatment, KPS, age, histology, and baseline cognitive functioning.

Intervention

Patients in the WBRT group will receive 4 Gy x 5 fractions in one week, which is a commonly utilized treatment schedule according to Dutch guidelines.
SRS will be performed with a Leksell Gamma Knife® Icon, Elekta Instruments, AB

(GKRS). Depending upon the volume, a dose of 18-25 Gy will be prescribed with 99-100% coverage of the target.

Study burden and risks

After randomisation (the minimisation method) patients will receive either WBRT (the standard treatment in the Netherlands for patients with >10 BM) or SRS.

Although SRS has been proven effective as the initial treatment option in patients with more than 10 BM, according to the Dutch guidelines, this is not a standard treatment.
WBRT consist of a series of treatments, usually 5 sessions in one week, unlike SRS, which is a one-day treatment. Patients randomised to WBRT will be treated at a radiation treatment center nearby their home address. While the MRI scan used for treatment planning is made at the Gamma Knife Center in Tilburg. A possible disadvantage might be that patients will be treated elsewhere.
According to study protocol MRI scans will occur every three months at the Gamma Knife Center.
Neuropsychological assessments (existing of six tests and three questionnaires) will take mental effort. To reduce this effort as much as possible, a shortened neuropsychological test battery was chosen (1,5 hour). Moreover, assessments will be combined with patients' hospital visits.

Ultimately, the purpose of this line of research is to assist both doctors and patients in individual decision-making with regard to the cognitive effects of treatment with either WBRT or SRS.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Contrast enhanced volumetric MRI-scan showing 11-20 newly diagnosed BM with a total tumor volume <= 30cc
• Lesion > 3 mm from optic apparatus*
• Patient age >= 18 years*
• Karnofsky Performance Status >= 70, WHO performance status <= 2*
• Anticipated survival (independent of the BM) greater than 3 months

Exclusion criteria

• No prior histologic confirmation of malignancy
• Primary brain tumor, lymphoma, small cell lung cancer, leukemia, or meningeal disease
• Progressive, symptomatic systemic disease without further treatment options
• Prior brain radiation or surgical resection of BM
• Additional history of a significant neurological or psychiatric disorder
• Participation in a concurrent study in which neuropsychological testing and/or health-related QOL assessments are involved
• Patients unable to complete test battery and/or study questionnaires due to any of the following reasons: lack of basic proficiency in Dutch, IQ below 85, severe aphasia, or paralysis

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-10-2016
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	12-08-2015
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-10-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-10-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-12-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-01-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL53447.028.15